Notice of Allowability	Application No.	Applicant(s)	
	08/529,767	SORGE ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *June 7, 2007*.

2. ☒ The allowed claim(s) is/are *33,35,37-40,42-46,49,52,54,56-72,75 and 77-83*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date 6/7/07
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

JEFFREY FREDMAN
PRIMARY EXAMINER
7/9/07

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on June 7, 2007 has been entered.

EXAMINER'S AMENDMENT

2. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Michael Albrecht on July 17, 2007.

The application has been amended as follows:

(Claim 14 was renumbered as claim 83).

Claims 1-32, 34, 36, 41, 47, 48, 50, 51, 53, 55, 73, 74 and 76 were cancelled.

33. A kit for the synthesis of a polynucleotide, said kit comprising:

a composition comprising:

(a) a first DNA polymerase, wherein said first polymerase possesses 3'-5' exonuclease activity and is thermostable, and

(b) a second DNA polymerase, wherein said second polymerase substantially lacks 3'-5' exonuclease activity and is thermostable;

wherein both the first DNA polymerase and the second DNA polymerase retain at least 50 percent of their specific activity after exposure to a temperature of 80 degrees Celsius for a period of 20 minutes.

35. A method of amplifying a polynucleotide sequence, said method comprising mixing a composition with a synthesis primer and a synthesis template, said composition comprising

(a) a first DNA polymerase possessing 3'-5' exonuclease activity, wherein said first polymerase is thermostable, and

(b) a second DNA polymerase, wherein said second polymerase substantially lacks 3'-5' exonuclease activity and is thermostable;

wherein both the first DNA polymerase and the second DNA polymerase retain at least 50 percent of their specific activity after exposure to a temperature of 80 degrees Celsius for a period of 20 minutes.

37. A method according to claim 35, wherein said first DNA polymerase is selected from the group consisting of *Pyrococcus furiosus* DNA polymerase, *Thermotoga maritima* DNA polymerase, *Thermococcus litoralis* DNA polymerase, and *Pyrococcus* GB-D DNA polymerase.

38. A method according to Claim 37, wherein said first DNA polymerase is *Pyrococcus furiosus* DNA polymerase.

39. A method according to Claim 35, wherein the second DNA polymerase is selected from the group consisting of *Thermus aquaticus* DNA polymerase, (exo-) *Thermococcus litoralis* DNA polymerase, (exo-) *Pyrococcus furiosus* DNA polymerase, and (exo-) *Pyrococcus* GB-D DNA polymerase.

40. A method according to Claim 35, wherein said second DNA polymerase is *Thermus aquaticus* DNA polymerase.

42. A method according to Claim 38, wherein said second DNA polymerase is *Thermus aquaticus* DNA polymerase.

43. A kit according to Claim 33, wherein said first DNA polymerase is selected from the group consisting of *Pyrococcus furiosus* DNA polymerase, *Thermotoga maritima* DNA polymerase, *Thermococcus litoralis* DNA polymerase, and *Pyrococcus* GB-D DNA polymerase.

44. A kit according to Claim 43, wherein said first DNA polymerase is *Pyrococcus furiosus* DNA polymerase.

45. A kit according to Claim 33, wherein the second DNA polymerase is selected from the group consisting of *Thermus aquaticus* DNA polymerase, (exo-) *Thermococcus litoralis* DNA polymerase, (exo-) *Pyrococcus furiosus* DNA polymerase, and (exo-) *Pyrococcus* GB-D DNA polymerase.

46. A kit according to Claim 45, wherein said second DNA polymerase is *Thermus aquaticus* DNA polymerase.

49. A kit according to Claim 33, said kit further comprising DNA primers.

52. A composition comprising:

(a) a first DNA polymerase, wherein said first polymerase possesses 3'-5' exonuclease activity and is thermostable, and

(b) a second DNA polymerase, wherein said second polymerase substantially lacks 3'-5' exonuclease activity and is thermostable;

wherein both the first DNA polymerase and the second DNA polymerase retain at least 50 percent of their specific activity after exposure to a temperature of 80 degrees Celsius for a period of 20 minutes.

54. A composition according to Claim 52, wherein said second DNA polymerase is *Thermus aquaticus* DNA polymerase.

56. A composition according to Claim 52, wherein said first DNA polymerase is selected from the group consisting of *Pyrococcus furiosus* DNA polymerase, *Thermotoga maritima* DNA polymerase, *Thermococcus litoralis* DNA polymerase, and *Pyrococcus* GB-D DNA polymerase.

57. A composition according to Claim 54, wherein said first DNA polymerase is *Pyrococcus furiosus* DNA polymerase.

58. A composition according to Claim 56, wherein said first DNA polymerase is *Thermococcus litoralis* DNA polymerase.

59. A composition according to Claim 56, wherein said first DNA polymerase is *Pyrococcus* GB-D DNA polymerase.

60. A composition according to Claim 56, wherein said first DNA polymerase is *Thermotoga maritima* DNA polymerase.

61. A composition according to Claim 58, wherein the second DNA polymerase is *Thermus aquaticus* DNA polymerase.

62. A composition according to Claim 58, wherein the second DNA polymerase is (exo-) *Thermococcus litoralis* DNA polymerase.

63. A composition according to Claim 58, wherein the second DNA polymerase is (exo-) *Pyrococcus furiosus* DNA polymerase.

64. A composition according to Claim 58, wherein the second DNA polymerase is (exo-) *Pyrococcus* GB-D DNA polymerase.

65. A composition according to Claim 59, wherein the second DNA polymerase is *Thermus aquaticus* DNA polymerase.

66. A composition according to Claim 59, wherein the second DNA polymerase is (exo-) *Thermococcus litoralis* DNA polymerase.

67. A competition according to Claim 59, wherein the second DNA polymerase is (exo-) *Pyrococcus furiosus* DNA polymerase.

68. A composition according to Claim 59, wherein the second DNA polymerase is (exo-) *Pyrococcus* GB-D DNA polymerase.

69. A composition according to Claim 60, wherein the second DNA polymerase is *Thermus aquaticus* DNA polymerase.

70. A composition according to Claim 60, wherein the second DNA polymerase is (exo-) *Thermococcus litoralis* DNA polymerase.

71. A composition according to Claim 60, wherein the second DNA polymerase is (exo-) *Pyrococcus furiosus* DNA polymerase.

72. A composition according to Claim 60, wherein the second DNA polymerase is (exo-) *Pyrococcus* GB-D DNA polymerase.

75. A method of synthesizing a polynucleotide sequence, said method comprising mixing a composition with a synthesis primer and a synthesis template, said composition comprising

(a) a first DNA polymerase possessing 3'-5' exonuclease activity, wherein said first polymerase is thermostable, and

(b) a second DNA polymerase, wherein said second polymerase substantially lacks 3'-5' exonuclease activity and is thermostable;

wherein both the first DNA polymerase and the second DNA polymerase retain at least 50 percent of their specific activity after exposure to a temperature of 80 degrees Celsius for a period of 20 minutes.

77. A method according to claim 75, wherein said first DNA polymerase is selected from the group consisting of *Pyrococcus furiosus* DNA polymerase, *Thermotoga maritima* DNA polymerase, *Thermococcus litoralis* DNA polymerase, and Pyrococcus GB-D DNA polymerase.

78. A method according to Claim 77, wherein said first DNA polymerase is *Pyrococcus furiosus* DNA polymerase.

79. A method according to Claim 75, wherein the second DNA polymerase is selected from the group consisting of *Thermus aquaticus* DNA polymerase, (exo-) *Thermococcus litoralis* DNA polymerase, (exo-) Pyrococcus furiosus DNA polymerase, and (exo-) Pyrococcus GB-D DNA polymerase.

80. A method according to Claim 75, wherein said second DNA polymerase is *Thermus aquaticus* DNA polymerase.

81. A method according to Claim 77, wherein the second DNA polymerase is selected from the group consisting of *Thermus aquaticus* DNA polymerase, (exo-) *Thermococcus litoralis* DNA polymerase, (exo-) *Pyrococcus furiosus* DNA polymerase, and (exo-) *Pyrococcus* GB-D DNA polymerase.

82. A method according to Claim 78, wherein said second DNA polymerase is *Thermus aquaticus* DNA polymerase.

83. A method according to claim 75, wherein the first DNA polymerase is selected from the group consisting of *Pyrococcus furiosus* DNA polymerase, ~~*Escherichia coli* DNA polymerase I, Klenow fragment, T-4 polymerase, T-7 polymerase,~~ ~~Vent polymerase~~ *Thermococcus litoralis* DNA polymerase, and ~~Deep Vent polymerase~~ *Pyrococcus* GB-D DNA polymerase.

3. The following is an examiner's statement of reasons for allowance: The claimed invention is novel and unobvious over the cited prior art. Several references will be specifically addressed.

The Zhu paper (Nucleic Acids Research (1991) 19(9)2511) teaches a mixture of the Taq DNA polymerase with exonuclease III. The claim, as amended, is not anticipated or rendered obvious by Zhu because the claim requires an exonuclease that

retains 50% activity at 80 C for 20 minutes. Exonuclease III is heat killed and inactive by 80C treatment for 20 minutes.

The Garrity reference teaches the use of Taq and Vent and Taq/Vent combinations, but never uses the two enzymes together in a single composition. All of the current claims require the two enzymes to be functional in a single composition. So when the Vent polymerase or Sequenase are used in first strand synthesis, the Vent or Sequenase are inactivated and removed by the ethanol precipitation prior to the addition of the Taq or Vent DNA polymerases. Consequently, Garrity does not anticipate the claimed composition because Garrity never teaches or suggests performing the method without the intervening ethanol precipitation and removal of this step would not have been obvious to the skilled practitioner at the time the invention was made.

The Livak reference also teaches Taq and Vent combinations, but also never uses the two enzymes together in a single composition. Livak first prepares a PCR product using Taq and then precipitates with isopropanol, washes with 70% ethanol before resuspending in TE and added the mixture to a tube containing Tli (or Vent) polymerase. So when the Taq polymerase is used in PCR, the Taq polymerase is inactivated and removed by the ethanol precipitation prior to the addition of the Vent DNA polymerases. Consequently, Livak does not anticipate the claimed composition because Livak never teaches or suggests performing the method without the intervening ethanol precipitation and removal of this step would not have been obvious to the skilled practitioner at the time the invention was made.

The Whitcomb reference uses a combination of Sequenase (which is a form of T7 DNA polymerase) and Taq polymerase, where random primed PCR is performed with Sequenase, followed by a purification step on a Sephacryl S-400 spin column, and then PCR using Taq. Whitcomb does not anticipate or render obvious the claim because the claim requires an exonuclease that retains 50% acitivty at 80C for 20 minutes. Sequenase is heat killed and inactive after this treatment. Further, it is unclear whether the Sequenase enzyme would be eluted from the S400 column under the conditions stated in Whitcomb.

Consequently, none of the prior art references teach or suggest the claims as amended above. For this reason, the claims are novel and unobvious over the prior art.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jeffrey Fredman
Primary Examiner
Art Unit 1637
7/24/07